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Incidence and Trends in Pediatric Malignancies Medulloblastoma/Primitive Neuroectodermal Tumor: A SEER Update

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Background. It has been suggested that cerebellar medulloblastoma (M) and primitive neuroectodermal tumors (PNET) arising elsewhere in the nervous system, represent a single entity (M/PNET), although this concept is controversial. Cancer registries permit population-based description of cases reported as medulloblastoma, those reported as PNET and description of the aggregate, M/PNET. ***Procedure.*** We reviewed the 768 cases of M/PNET (633 diagnosed medulloblastoma and 135 diagnosed PNET) among persons under 20 years of age in the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database. ***Results.*** The incidence of M/PNET rose 23%, from 4 per 10^6 person-years in 1973–77 to 4.9 per 10^6 person-years in 1993–98. Cases reported as PNET were more likely than those reported as medulloblastoma to be supratentorial (30.4% vs. 1.9%, $P < 0.001$) and to be female (42.2% vs. 35.4%, $P = 0.13$). The difference in 5-year survival between the 600 children with infratentorial medulloblastoma vs. the 49 children with infratentorial PNET was not statistically significant (55% vs. 43%). Regardless of reporting diagnosis, survival was poorer among children age 0–3 years and those with supratentorial tumors. Children diagnosed in the more recent period from 1985–1998 had a longer median survival than children diagnosed in 1973–84 (4.9 years vs. 10 years, $P < 0.05$). Rates were 42% higher among Whites compared to Blacks ($4.5/10^6$ person-years vs. $3.1/10^6$ person-years, $P < 0.01$). ***Conclusions.*** We found M/PNET is increasing in incidence and more frequent among Whites. Given that medulloblastoma and PNET are histologically identical and have similar epidemiologic profiles, future studies should provide analyses that combine these entities. Med Pediatr Oncol 2002;39:190–194.

Key words: medulloblastoma; primitive neuroectodermal tumor; epidemiology; SEER

INTRODUCTION

Brain tumors are the most common type of solid tumor in children [1]. Tumors diagnosed as either medulloblastoma or primitive neuroectodermal tumor (M/PNET) represent 10–20% of the brain tumors seen in this age group [2]; although such tumors can occur in adults, they are uncommon.

Much of the current knowledge regarding epidemiology of childhood M/PNET is based on case series from one or more clinical institutions. Such series may suffer from ascertainment biases when enrolled patients are not representative of the general population of children with illness. There are few population-based studies of M/PNETs. These tumors were included as part of an epidemiologic review of all pediatric cancers [3], but it has been a decade since the last comprehensive study of M/PNET [4]. Since then, cancer registries have accumulated many cases of M/PNET, the nosology has been under revision, and treatment approaches have reportedly enhanced survival. For these reasons, we here describe extant population-based data on M/PNET.

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MATERIALS AND METHODS

The National Cancer Institute's Surveillance, Epidemiology and End Results program (SEER) collects data from all persons diagnosed with cancer who are residents of collaborating states or localities. In these jurisdictions, reporting to cancer registries is legally mandated [5]. We used data on M/PNET from the nine registries that

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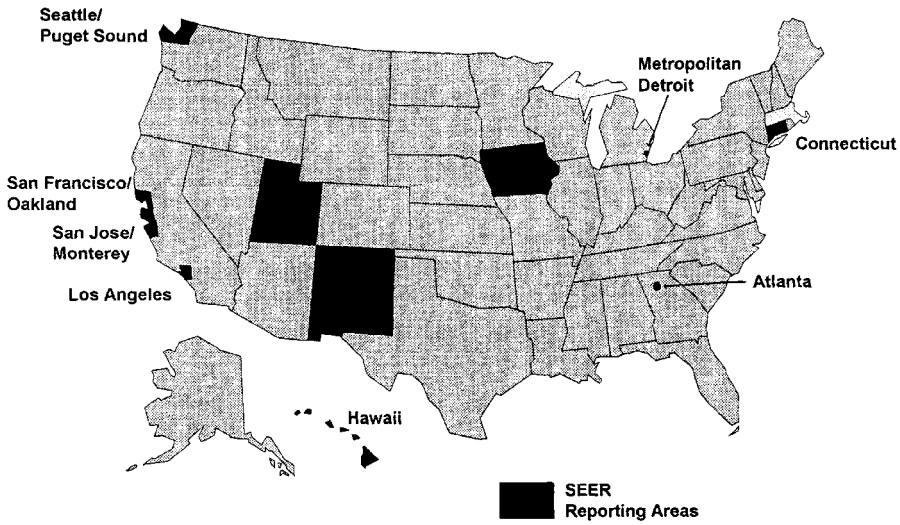

Fig. 1. Surveillance, epidemiology, and end results program.

have collaborated with SEER since 1973: Connecticut, Hawaii, Iowa, New Mexico, Utah, Atlanta, Detroit, Seattle/Puget Sound, and San Francisco/Oakland (Fig. 1). Reporting has been estimated to be 98% complete or better in each of these registries [6]. SEER data include tumor site, histology, and demographics. Patients are regularly followed-up both locally and with the National Death Index [7] to ascertain survival status.

We included all persons under 20 years of age with brain tumors (C71.0–C71.9) diagnosed from 1973 to 1998, and histologically reported as medulloblastoma (M-9470) or PNET (M-9473) as coded by the International Classification of Diseases for Oncology, version 2 [8]. Excluded from analysis were patients with multiple primaries, those cases diagnosed at autopsy or documented by death certificate only and patients without at least 1 month of follow up.

Incidence rates were calculated using SEER*Stat software [9] and expressed as cases per million person-years among the population under 20 years old. Incidence rates were compared under the assumption that the number of incidents follows a Poisson distribution. Simple proportions were tested for statistical significance using the Chi-square test. Observed survivals (from all causes) were calculated using life-table methods (in yearly intervals). Patients were censored at the time of loss to follow-up or December 31, 1998, whichever occurred first. Log-rank type of tests were employed to compare survival curves [10]. SAS software package was used for all comparisons [11]. All *P*-values reflect two-sided tests.

RESULTS

There were 768 children who had the diagnosis of M/PNET (Table I). The relative proportion of medulloblastoma and PNET contributing to the total M/PNET changed over the period from 1973–98 (Fig. 2). PNET was rarely diagnosed prior to 1986; since that time the frequency increased and for the years 1993–98, PNET represented 33% of M/PNET. Contemporaneous with increased PNET reporting, there was a decline in diagnosis of medulloblastoma, but overall rates of M/PNET rose 23% from 4.0 per 10^6 person-years in 1973–77 to 4.9 per 10^6 person-years in 1993–98. Rates were 42% higher among Whites compared to Blacks ($4.5/10^6$ person-years vs. $3.1/10^6$ person-years, $P < 0.01$).

For the 768 patients with M/PNET, 135 were reported as PNET and 633 were reported as medulloblastoma. There was an overall male predominance (2:1). Cases reported as PNET were more likely to be supraten-

Table I. Medulloblastoma/PNET Descriptive Factors

Age	
00–03	244 (32%)
04–09	315 (41%)
10–14	140 (18%)
15–19	69 (9%)
All ages	768
Gender	
Male(%)	487 (63%)
Female(%)	281 (37%)
Ethnicity	
White	626 (82%)
Black	70 (9%)
Other	72 (9%)
Anstomic location	
Supratentorial	53 (7%)
Infratentorial	649 (85%)
Mixed/overlapping	21 (3%)
Brain, NOS	45 (6%)

The percentages may not add to 100% due to rounding.

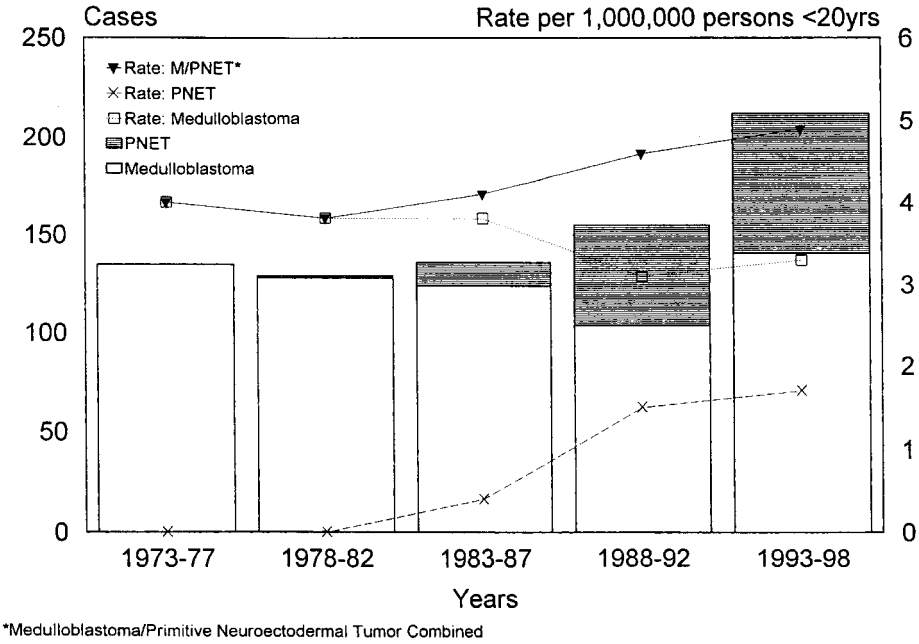

Fig. 2. Cases and rates of medulloblastoma, PNET, and M/PNET.

torial than those reported as medulloblastoma (30.4% vs. 1.9%, $P < 0.001$), and to be female (42.2% vs. 35.4%, $P < 0.001$).

Median survival among children with M/PNET varied by patient age, site of tumor, histology, and time period of diagnosis (Table II), but there were no significant differences in survival by race or gender ($P > 0.05$). Among the 768 children with M/PNET, those aged 0–3 years had the worse survival of the different age groups ($P < 0.001$), (Table II and Fig. 3). Children diagnosed with supratentorial M/PNET had poorer survival than children with infratentorial M/PNET ($P < 0.01$). The 633 children diagnosed with medulloblastoma had a better median survival than the 135 children diagnosed with PNET (7.2 years vs. 2.5 years), and this was also true when limited to infratentorial tumors (medulloblastoma n = 600, 7.5 years vs. PNET n = 49, 2.8 years). However, because the diagnosis of PNET reflects recent nosologic change, the cases reported as such had far shorter follow-up times and fewer deaths; the survival differences were not found to be statistically significant ($P = 0.5$). Children diagnosed in the more recent period from 1985–1998 had a longer median survival than children diagnosed in 1973–84 (4.9 years vs. 10 years, $P < 0.05$).

CONCLUSIONS

Our review of 768 children with M/PNET reported to a population-based registry is the largest collection of these patients. More important, this collection does not suffer from the ascertainment biases inherent in institutionally-based series that reflect patient referral patterns. Here we updated the information available from the SEER registry and focused on M/PNET, as has not been done previously [3]. Previous epidemiologic work used the International Classification of Childhood Cancer System [3], while we have elected to use the ICD system to facilitate comparisons with extant case series. Our PNET category does not include intracranial neuroblastoma or pineoblastoma, both of which were included in the PNET category in the SEER Monograph [3]. We present age-adjusted M/PNET incidence rates for 1973–1998 to show the trend over time, the most recent

Table II. Medulloblastoma/PNET Survival

	n	1 year	5 year	Median
Age				
0–3 years	244	62%	39%	1.8 years
4–9 years	315	86%	58%	>10 years
10–14 years	140	88%	58%	7.4 years
15–19 years	69	93%	65%	9.8 years
All Ages	768	79%	53%	6.3 years
Gender				
Male	487	81%	51%	5.6 years
Female	281	76%	55%	7 years
Year of Diagnosis				
1973–1984	331	79%	50%	4.9 years
1985–1998	455	80%	56%	>10 years
Site of tumor				
Supratentorial	53	67%	35%	2.4 years
Infratentorial	649	81%	55%	7.2 years
Mixed/Overlapping	21	90%	63%	>10 years
Brain, NOS	45	70%	41%	2.8 years

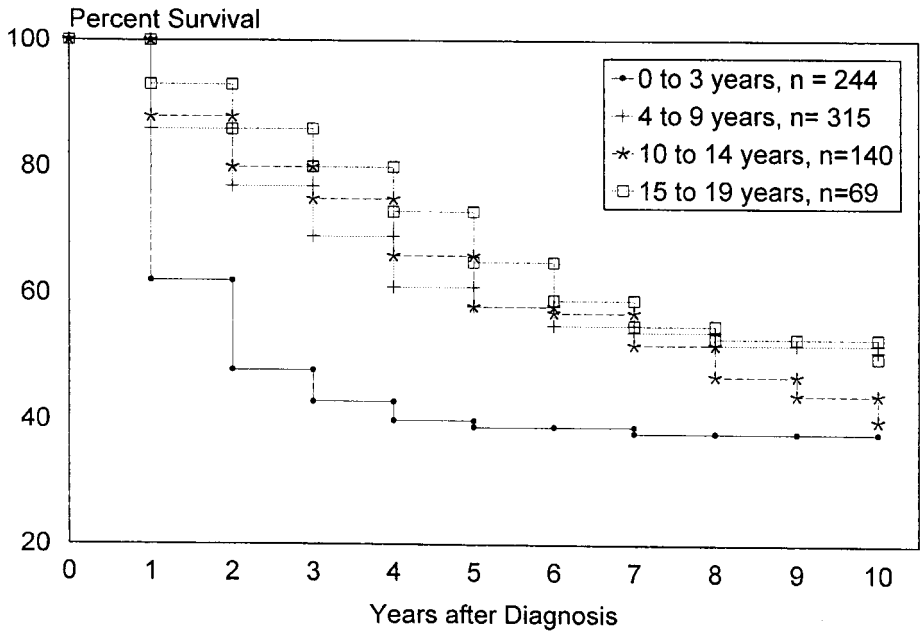

Fig. 3. Age-specific survival for medulloblastoma/primitive neuroectodermal tumor.

rates having been previously reported though using a different classification method [3].

Many of our findings affirm previous reports of M/PNET [4,12,13], e.g., the overall male predominance (2:1), young age at diagnosis (72% less than 10 years old at diagnosis) and a predominantly infratentorial location (> 80%), which is associated with a better 5-year survival than supratentorial location (55% vs. 35%). New findings include an absolute increase in the incidence of M/PNET, a statistically significant difference in incidence rates between Whites and Blacks and an increase in median survival for recent years. (Note that this study reports incidence among persons under 20 years old while an earlier publication [4] reports incidence for all ages.) While the increase in M/PNET diagnoses may reflect to some extent, improvement in diagnostic ability due to enhanced neuroimaging capability, the absolute increase in incidence of the combined entities (M/PNET) is a real finding, untainted by the ongoing debate over nosology.

While cancer registry data provide large numbers of cases and freedom from ascertainment biases, these data also present limitations. There was no uniform microscopic review; we can only analyze the data reported to the registries, which in turn is based upon diagnoses rendered by multiple pathologists with variable expertise. Nosologic issues relating to the entities medulloblastoma and PNET continue to occupy neuropathologists [14–17], so these findings reflect the state of practice if not the state of the art. For example, among children with medulloblastoma or PNET, those aged 0–3 years have the shortest median survival. This may be related to misclassification of atypical teratoid/rhabdoid tumors as M/PNET; prognosis for the former entity is grave [18]. Because this study did not collect tissue for independent review, we are unable to measure this potential source of misclassification.

Cancer registries offer clinicians an overview of disease unobtainable by hospital-based case series. As the biology of M/PNET becomes better defined through use of immunohistochemistry and molecular genetics, neuropathologic diagnosis will likely become more precise—as will the derivative cancer registry data. For meantime, given that medulloblastoma and PNET are histologically identical and have similar epidemiologic profiles, future studies should provide analyses that combine these entities.

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